FILE 'HOME' ENTERED AT 09:16:58 ON 21 NOV 2002

=> file medline biosis caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 09:17:09 ON 21 NOV 2002

FILE 'BIOSIS' ENTERED AT 09:17:09 ON 21 NOV 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'CAPLUS' ENTERED AT 09:17:09 ON 21 NOV 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

=> s antisense (9a) ras
L1 562 ANTISENSE (9A) RAS

=> s antisense (9a) (ras or hras or kiras or kras)
L2 564 ANTISENSE (9A) (RAS OR HRAS OR KIRAS OR KRAS)

=> s l2 and chemotherap?
L3 18 L2 AND CHEMOTHERAP?

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 13 DUP REM L3 (5 DUPLICATES REMOVED)

=> d 1-13 ti

L4 ANSWER 1 OF 13 MEDLINE DUPLICATE 1
TI Farnesyl transferase inhibitors: a major breakthrough in anticancer therapy? Naples, 12 April 2002.

L4 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2002 ACS
TI Inhibitors of Ras protein prenyl transferase for antitumor application

L4 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2002 ACS
TI Inhibitors of prenyl-protein transferase

L4 ANSWER 4 OF 13 MEDLINE DUPLICATE 2
TI A Phase I trial of H-**ras antisense** oligonucleotide ISIS 2503 administered as a continuous intravenous infusion in patients with advanced carcinoma.

L4 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2002 ACS
TI Antisense therapeutics: Lessons from early clinical trials

L4 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2002 ACS
TI Antisense oligonucleotides blocking synthesis of the R1 and R2 components of ribonucleotide reductase for treatment of cancer

L4 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2002 ACS
TI Combination of radiotherapy and anti-angiogenic factors for cancer therapy

L4 ANSWER 8 OF 13 MEDLINE DUPLICATE 3
TI Chronic myelogenous leukemia: biology and therapy.

L4 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2002 ACS
TI Modified **antisense** oligodeoxyribonucleotides complementary to

human Ha-**ras** gene and their therapeutic use

L4 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2002 ACS
TI Sensitization of tumor cells to radiation and **chemotherapy** with ras pathway protein product inhibitors

L4 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2002 ACS
TI Antisense oligonucleotides to the androgen receptor and acidic fibroblast growth factor in **chemotherapy** of benign hyperplasia or prostate cancer

L4 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2002 ACS
TI Combination of antineoplastic agent and antisense oligonucleotides for treatment of cancer

L4 ANSWER 13 OF 13 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI ANTISENSE FOS OLIGODEOXYRIBONUCLEOTIDES SUPPRESS THE GENERATION OF CHROMOSOMAL ABERRATIONS.

=> d 12 bib ab

L4 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2002 ACS
AN 1994:499787 CAPLUS
DN 121:99787
TI Combination of antineoplastic agent and antisense oligonucleotides for treatment of cancer
IN Calabretta, Bruno; Skorski, Thomasz
PA Temple University - of the Commonwealth System of High Education, USA; Thomas Jefferson University
SO PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9408625	A1	19940428	WO 1993-US7541	19930810
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2147663	AA	19940428	CA 1993-2147663	19930810
	AU 9350050	A1	19940509	AU 1993-50050	19930810
	EP 668782	A1	19950830	EP 1993-919965	19930810
	EP 668782	B1	20010411		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 08506087	T2	19960702	JP 1993-509970	19930810
	AT 200427	E	20010415	AT 1993-919965	19930810
PRAI	US 1992-965671	A2	19921021		
	WO 1993-US7541	W	19930810		

AB Therapeutic combinations of an antisense oligonucleotide and another, non-oligonucleotide **chemotherapeutic** agent allow for a reduced dosage of the non-oligonucleotide agent, and hence, reduced toxicity to the host. The antisense oligonucleotide is directed against the transcript of a target oncogene or proto-oncogene assocd. with the particular neoplastic disease under treatment. The combination is particularly useful in treating leukemias, more particularly as a bone marrow purging agent. Mafosfamide inhibited the growth of CML marrow cells more effectively than healthy marrow cells in vitro; at a concn. of 100 .mu.M mafosfamide selectively killed CML marrow cells in mixed culture. When used in combination with an antisense oligonucleotide to the c-abl gene, the differential in killing of healthy and CML cells was much greater. Comparable results were found when the expt. was repeated

in SCID mice.

=> d 12 kwic

L4 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2002 ACS
AB Therapeutic combinations of an antisense oligonucleotide and another, non-oligonucleotide **chemotherapeutic** agent allow for a reduced dosage of the non-oligonucleotide agent, and hence, reduced toxicity to the host. The antisense oligonucleotide. . .
IT Alkylating agents, biological
(as neoplasm inhibitor, synergism in cancer **chemotherapy** with antisense oligonucleotides of)
IT Alkaloids, biological studies
Hormones
Nitrogen mustards
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as neoplasm inhibitor, synergism in cancer **chemotherapy** with antisense oligonucleotides of)
IT Bone marrow
(purging of neoplastic cells from, oncogene antisense oligonucleotides and **chemotherapeutic** agents in)
IT Gene, animal
RL: BIOL (Biological study)
(L-myc, antisense oligonucleotides to, synergism in cancer **chemotherapy** with neoplasm inhibitors of)
IT Gene, animal
RL: BIOL (Biological study)
(N-myc, antisense oligonucleotides to, synergism in cancer **chemotherapy** with neoplasm inhibitors of)
IT Gene, animal
RL: BIOL (Biological study)
(N-**ras**, **antisense** oligonucleotides to, synergism in cancer **chemotherapy** with neoplasm inhibitors of)
IT Gene, animal
RL: BIOL (Biological study)
(TP53, antisense oligonucleotides to, synergism in cancer **chemotherapy** with neoplasm inhibitors of)
IT Nutrients
(anti-, as neoplasm inhibitor, synergism in cancer **chemotherapy** with antisense oligonucleotides of)
IT Gene, animal
RL: BIOL (Biological study)
(bcr-c-abl, antisense oligonucleotides to, synergism in cancer **chemotherapy** with neoplasm inhibitors of)
IT Gene, animal
RL: BIOL (Biological study)
(c-Ha-**ras**, **antisense** oligonucleotides to, synergism in cancer **chemotherapy** with neoplasm inhibitors of)
IT Gene, animal
RL: BIOL (Biological study)
(c-Ki-**ras**, **antisense** oligonucleotides to, synergism in cancer **chemotherapy** with neoplasm inhibitors of)
IT Gene, animal
RL: BIOL (Biological study)
(c-abl, antisense oligonucleotides to, synergism in cancer **chemotherapy** with neoplasm inhibitors of)
IT Gene, animal
RL: BIOL (Biological study)
(c-erbB, antisense oligonucleotides to, synergism in cancer

chemotherapy with neoplasm inhibitors of)

IT Gene, animal
RL: BIOL (Biological study)
(c-erbB2, antisense oligonucleotides to, synergism in cancer **chemotherapy** with neoplasm inhibitors of)

IT Gene, animal
RL: BIOL (Biological study)
(c-fos, antisense oligonucleotides to, synergism in cancer **chemotherapy** with neoplasm inhibitors of)

IT Gene, animal
RL: BIOL (Biological study)
(c-kit, antisense oligonucleotides to, synergism in cancer **chemotherapy** with neoplasm inhibitors of)

IT Gene, animal
RL: BIOL (Biological study)
(c-myb, antisense oligonucleotides to, synergism in cancer **chemotherapy** with neoplasm inhibitors of)

IT Gene, animal
RL: BIOL (Biological study)
(c-myc, antisense oligonucleotides to, synergism in cancer **chemotherapy** with neoplasm inhibitors of)

IT Deoxyribonucleic acids
RL: BIOL (Biological study)
(complementary, antisense, to oncogenes, in combination with antineoplastics, for **chemotherapy** of cancer)

IT Deoxyribonucleic acid formation factors
RL: BIOL (Biological study)
(cyclins, gene for, antisense oligonucleotides to, synergism in cancer **chemotherapy** with neoplasm inhibitors of)

IT Phosphoproteins
RL: BIOL (Biological study)
(cyclins D1, gene for, antisense oligonucleotides to, synergism in cancer **chemotherapy** with neoplasm inhibitors of)

IT Therapeutics
(geno-, of cancer, antisense oncogenes in, synergism with **chemotherapeutic** neoplasm inhibitors in relation to)

IT Neoplasm inhibitors
(leukemia, oncogene antisense oligonucleotides and **chemotherapeutic** agents in)

IT Nucleotides, biological studies
RL: BIOL (Biological study)
(oligo-, alkylphosphonate-linked, antisense to oncogenes, in combination with antineoplastics, for **chemotherapy** of cancer)

IT Nucleotides, biological studies
RL: BIOL (Biological study)
(oligo-, thiophosphate-linked, antisense to oncogenes, in combination with antineoplastics, for **chemotherapy** of cancer)

IT Neoplasm inhibitors
(synergistic, oncogene antisense oligonucleotides and **chemotherapeutic** agents in)

IT Gene
RL: BIOL (Biological study)
(transforming, antisense oligonucleotides to, synergism in cancer **chemotherapy** with neoplasm inhibitors of)

IT 136857-41-5, DNA (human bcr-abl transcript antisense oligonucleotide)
146485-63-4, DNA (human bcr-abl transcript antisense oligonucleotide)
146485-64-5, DNA (human bcr-abl transcript antisense oligonucleotide)
146485-65-6, DNA (human bcr-abl transcript antisense oligonucleotide)
146485-66-7, DNA (human bcr-abl transcript antisense oligonucleotide)
146485-67-8, DNA (human bcr-abl transcript antisense oligonucleotide)
146485-68-9, DNA (human bcr-abl transcript antisense oligonucleotide)
146485-69-0, DNA (human bcr-abl transcript antisense oligonucleotide)

146485-70-3, DNA (human bcr-abl transcript antisense oligonucleotide)
146485-71-4, DNA (human bcr-abl transcript antisense oligonucleotide)
146485-72-5, DNA (human bcr-abl transcript antisense oligonucleotide)
146485-73-6, DNA (human bcr-abl transcript antisense oligonucleotide)
146485-74-7, DNA (human bcr-abl transcript antisense oligonucleotide)
146485-75-8, DNA (human bcr-abl transcript antisense oligonucleotide)
146485-76-9, DNA (human bcr-abl transcript antisense oligonucleotide)
146485-77-0, DNA (human bcr-abl transcript antisense oligonucleotide)
146485-78-1, DNA (human bcr-abl transcript antisense oligonucleotide)
146485-79-2, DNA (human bcr-abl transcript antisense oligonucleotide)
146485-80-5, DNA (human bcr-abl transcript antisense oligonucleotide)
146485-81-6, DNA (human bcr-abl transcript antisense oligonucleotide)
146485-82-7, DNA (human bcr-abl transcript antisense oligonucleotide)
156533-77-6, DNA (human bcr-abl transcript antisense oligonucleotide)
RL: BIOL (Biological study)
(antisense oligonucleotide to bcr-abl, as neoplasm inhibitor, synergism with **chemotherapeutic** agents in relation to)

IT 121938-12-3, DNA (human c-myb transcript antisense oligonucleotide)
RL: BIOL (Biological study)
(antisense oligonucleotide to c-myb, as neoplasm inhibitor, synergism with **chemotherapeutic** agents in relation to)

IT 50-07-7, Mitomycin C 50-44-2, 6-Mercaptopurine 50-76-0, Actinomycin D 50-91-9, 5-Fluorodeoxyuridine 51-21-8, 5-Fluorouracil 52-24-4, Triethylenethiophosphoramide 53-03-2 55-98-1, Busulfan 56-53-1, Diethylstilbestrol 57-22-7, Vincristine 58-22-0, Testosterone 59-05-2, Methotrexate 68-96-2, Hydroxyprogesterone 127-07-1, Hydroxyurea 147-94-4, Cytosine arabinoside 148-82-3, Melphalan 154-42-7, 6-Thioguanine 154-93-8, Bis-chloroethylnitrosourea 305-03-3, Chlorambucil 320-67-2, 5-Azacytidine 645-05-6, Hexamethylmelamine 671-16-9, Procarbazine 865-21-4, Vinblastine 3778-73-2, Ifosfamide 4342-03-4, Dacarbazine 10540-29-1, Tamoxifen 11056-06-7, Bleomycin 13010-47-4, Ccnu 13909-09-6, Meccnu 15663-27-1 16268-62-5, Pentamethylmelamine 18378-89-7, Mithramycin 20830-81-3, Daunomycin 23214-92-8, Doxorubicin 29767-20-2, Teniposide 33419-42-0 51264-14-3, Amsacrine 52128-35-5, Trimetrexate 53643-48-4, Vindesine 53910-25-1, Deoxycoformycin 56420-45-2, Epirubicin 58957-92-9, Idarubicin 62435-42-1, 4-HC 63521-85-7, Esorubicin 65271-80-9, Mitoxantrone 88859-04-5, Mafosfamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as neoplasm inhibitor, synergism in cancer **chemotherapy** with antisense oligonucleotides of)

=> d 4 bib ab

L4 ANSWER 4 OF 13 MEDLINE DUPLICATE 2
AN 2001523932 MEDLINE
DN 21455255 PubMed ID: 11571742
TI A Phase I trial of H-**ras antisense** oligonucleotide ISIS 2503 administered as a continuous intravenous infusion in patients with advanced carcinoma.
AU Cunningham C C; Holmlund J T; Geary R S; Kwoh T J; Dorr A; Johnston J F; Monia B; Nemunaitis J
CS U.S. Oncology, Dallas, Texas, USA.. Casey.Cunningham@usoncology.com
SO CANCER, (2001 Sep 1) 92 (5) 1265-71.
Journal code: 0374236. ISSN: 0008-543X.
CY United States
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Journal; Article; (JOURNAL ARTICLE)

LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200110
ED Entered STN: 20010926
Last Updated on STN: 20011008
Entered Medline: 20011004
AB BACKGROUND: Abnormal expression of Ras proteins frequently is found with oncogenic transformation making ras a promising therapeutic target. ISIS 2503 is a 20-base **antisense** phosphorothioate oligodeoxyribonucleotide that specifically downregulates H-**ras** expression and inhibits tumor cell growth in preclinical studies. Here, the authors report an initial clinical study of the safety and tolerability of an intravenous infusion of ISIS 2503 in patients with advanced cancer. METHODS: A continuous intravenous infusion of ISIS 2503 was administered for 14 days every 3 weeks to 23 patients with a variety of solid tumors refractory to standard therapy. The dose of ISIS 2503 was increased in sequential cohorts of patients, as toxicity allowed, until a final dose of 10.0 mg/kg/day of body weight was reached. Toxicity was scored by the National Cancer Institute's Common Toxicity Criteria, and tumor response was monitored after every two treatment cycles. Pharmacokinetic studies were performed in some of the patients up to, and including, the final dose of 10 mg/kg/day/day of body weight. Levels of H-ras mRNA expression also were determined in the circulating lymphocytes of some patients by quantitative reverse transcriptase-polymerase chain reaction. RESULTS: A total of 23 patients received 63 cycles of ISIS 2503 at escalating doses to 10.0 mg/kg/day without dose-limiting toxicity and only minimal side effects. Four patients had stabilization of their disease for 6-10 cycles. No consistent decreases in H-ras mRNA levels were observed in peripheral blood lymphocytes. CONCLUSIONS: ISIS 2503, an **antisense** oligonucleotide against H-**ras**, was well tolerated as a single agent at doses up to 10.0 mg/kg/day by 14-day continuous intravenous infusion. Several patients had stabilization of disease, suggesting that ISIS 2503 had some tumor growth inhibitory effects and future trials of ISIS 2503 in combination with **chemotherapy** should be considered.

=> d 6 bib ab

L4 ANSWER 6 OF 13 CAPLUS
AN 2000:573929 CAPLUS
DN 133:172162
TI Antisense oligonucleotides blocking synthesis of the R1 and R2 components of ribonucleotide reductase for treatment of cancer
IN Wright, Jim A.; Young, Aiping H.
PA Genesense Technologies Inc., Can.
SO PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000047733	A1	20000817	WO 2000-CA120	20000209

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,

DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6121000	A	20000919	US 1999-249730	19990211
BR 2000008788	A	20011106	BR 2000-8788	20000209
EP 1153128	A1	20011114	EP 2000-903456	20000209

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRAI US 1999-249730	A	19990211	
WO 2000-CA120	W	20000209	

AB Compds. and methods for modulating cell proliferation, preferably inhibiting the proliferation of tumor cells are described. Compds. that may be used to modulate cell proliferation include antisense oligonucleotides complementary to regions of the mammalian ribonucleotide reductase genes. The R2 component of the enzyme was found to play a role in the Ha-ras dependent transformation as the frequency of focus formation was greater in cells with constitutive expression of R2 than in control cells. Hydroxyurea resistance was found to be assocd. with increased levels of ribonucleotide reductase in L cells. Selection of antisense DNAs is described.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT